

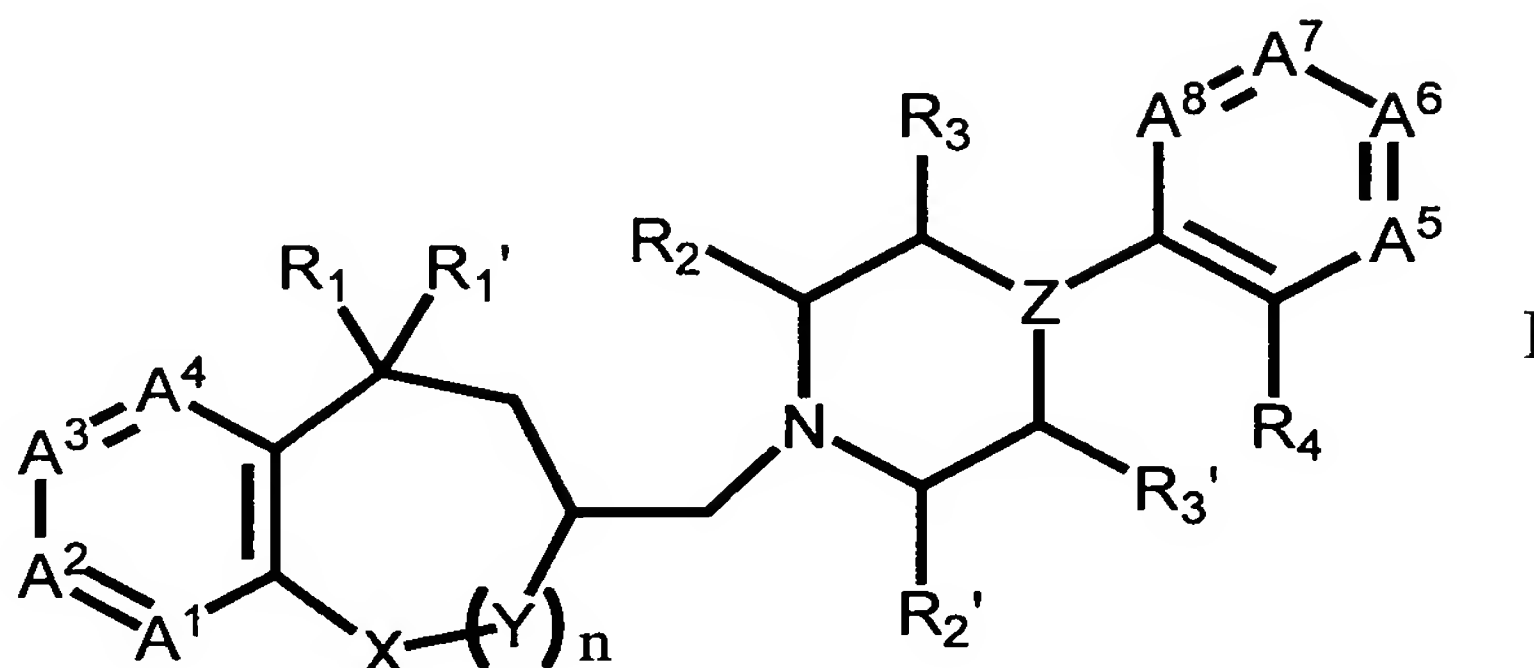
AMENDMENTS TO THE CLAIMS

Please cancel Claims 1-29 without prejudice and insert therefore new Claims 30-48. This listing of claims will replace all prior versions, and listings, of claims in the application.

Listing of Claims:

Claims 1-29 (canceled)

30. (New) A compound of the formula I:



wherein:

A^1 , A^2 , A^3 and A^4 each independently represent $-C(R_5)-$ or $-N-$, provided that at least one of A^1 , A^2 , A^3 and A^4 is $-N-$;

A^5 , A^6 , A^7 and A^8 each independently represent $-C(R_6)-$ or $-N-$;

R_1 and R_1' each independently represent a hydrogen atom, a halogen atom, a hydroxyl group, a cyano group, a C_{1-6} alkyloxy group, a C_{1-6} alkyloxyalkyloxy group, a C_{1-6} alkyloxycarbonyl group, a C_{1-6} alkyloxycarbonylamino group, a C_{1-6} alkylcarbonyl group, a C_{1-6} alkylcarbonyloxy group, a C_{1-6} alkylcarbonylamino group, a C_{1-6} alkylsulfonyl group, a C_{1-6} alkylsulfonylamino group, a C_{1-6} alkylsulfonyl- C_{1-6} alkylamino group, a carbamoylamino group, a $(C_{1-6}$ alkyl)carbamoylamino group, a di(C_{1-6} alkyl)carbamoylamino group, a pyrazolyl group, a triazolyl group, an oxazolyl group, or a C_{1-6} alkyl group optionally having a substituent selected from the following group α ; or R_1 and R_1' together form an oxo group or a C_{1-3} alkylene ketal group;

R_2 represents a hydrogen atom or a C_{1-6} alkyl group optionally having a hydroxyl group, or R_2 and R_2' or R_3' together form a C_{1-3} alkylene group or an oxy- C_{1-3} alkylene group;

R_2' represents a hydrogen atom or a C_{1-6} alkyl group optionally having a hydroxyl group, or R_2' and R_2 or R_3 together form a C_{1-3} alkylene group or an oxy- C_{1-3} alkylene group;

R_3 represents a hydrogen atom, a hydroxyl group, a halogen atom, a C_{1-6} alkyloxy group, a C_{1-6} alkylcarbonyl group, a C_{1-6} alkyloxycarbonyl group, a C_{1-6} alkylsulfonyl group, a C_{1-6} alkylsulfonylamino group, a C_{1-6} alkylsulfonylalkylamino group, a cyano group, or a C_{1-6} alkyl group optionally having a substituent selected from the group α ; or R_3 and R_3' or R_2' together form a C_{1-3} alkylene group or an oxy- C_{1-3} alkylene group;

R_3' represents a hydrogen atom, a hydroxyl group, a halogen atom, a C_{1-6} alkyloxy group, a C_{1-6} alkylcarbonyl group, a C_{1-6} alkyloxycarbonyl group, a C_{1-6} alkylsulfonyl group, a C_{1-6} alkylsulfonylamino group, a C_{1-6} alkylsulfonylaminoalkyl group, a cyano group, or a C_{1-6} alkyl group optionally having a substituent selected from the group α ; or R_3' and R_3 or R_2 together form a C_{1-3} alkylene group or an oxy- C_{1-3} alkylene group;

R_4 represents a hydrogen atom, a halogen atom, a C_{1-6} alkyl group optionally having a hydroxyl group, a halogeno- C_{1-6} alkyl group, a C_{1-6} alkyloxy- C_{1-6} alkyl group, a C_{1-6} alkylcarbonyl group, a cyano group, a formyl group, a C_{1-6} alkyloxycarbonyl group, a C_{1-6} alkylcarbonylamino group, a C_{1-6} alkylcarbonyl- C_{1-6} alkylamino group or a C_{1-6} alkylsulfonyl group; or when Z is $-C(R_7)-$, then R_4 and R_7 together form $-C(R_8)(R_8')-O-$, $-C(R_8)(R_8')-CO-$, $-C(R_8)(R_8')-C(R_8)(R_8')-$, $-O-CO-$, $-CO-O-$, $-CO-C(R_8)(R_8')-$, $-O-C(R_8)(R_8')-$, $-CH(R_8)-N(R_9)-$ or $-N(R_9)-CH(R_8)-$;

R_5 represents a hydrogen atom, a hydroxyl group, a fluorine atom, a chlorine atom, a C_{1-6} alkyl group, a C_{1-6} alkylamino group, a C_{1-6} alkylcarbonyl group, a C_{1-6} alkylcarbonylamino group, a C_{1-6} alkylcarbonyl- (C_{1-6}) alkylamino group, or a cyano group;

R_6 represents a hydrogen atom, a halogen atom, a C_{1-6} alkyl group optionally having a hydroxyl group, a halogeno- C_{1-6} alkyl group, a C_{1-6} alkyloxy- C_{1-6} alkyl group, a C_{1-6} alkylcarbonyl group, a cyano group, a formyl group, a C_{1-6} alkyloxycarbonyl group, a C_{1-6} alkylcarbonylamino group, a C_{1-6} alkylcarbonyl- C_{1-6} alkylamino group, or a C_{1-6} alkylsulfonyl group;

R_7 represents a hydrogen atom, a halogen atom, a cyano group, a C_{1-6} alkyl group, a C_{1-6} alkyloxy group; or R_7 and R_4 together form $-C(R_8)(R_8')-O-$, $-C(R_8)(R_8')-CO-$, $-C(R_8)(R_8')-C(R_8)(R_8')-$, $-O-CO-$, $-CO-O-$, $-CO-C(R_8)(R_8')-$, $-O-C(R_8)(R_8')-$, $-CH(R_8)-N(R_9)-$ or $-CH(R_8)-N(R_9)-$;

R_8 and R_8' each independently represent a hydrogen atom, a hydroxyl group, a C_{1-6} alkyl group optionally having a hydroxyl group, or a C_{1-6} alkylsulfonyl group;

R_9 represents a hydrogen atom, a C_{1-6} alkyl group, a C_{1-6} alkylsulfonyl group, a C_{1-6} alkyloxycarbonyl group, or a formyl group;

R_a represents a hydrogen atom, a C_{1-6} alkyl group, a C_{1-6} alkyloxycarbonyl group, a carbamoyl group, a (C_{1-6} alkyl)carbamoyl group, a di(C_{1-6} alkyl)carbamoyl group, a C_{1-6} alkylsulfonyl group, a pyrazolyl group, a triazolyl group, or an oxazolyl group;

X represents $-CH_2-$, $-CH(OH)-$, $-N(R_a)-$, $-O-$, $-S-$ or $-SO_2-$;

Y represents $-CH_2-$ or $-N(R_a)-$;

Z represents $-C(R_7)-$ or $-N-$;

n indicates an integer of 0 or 1;

group α is selected from the group consisting of: a halogen atom, a hydroxyl group, a C_{1-6} alkylcarbonyl group, a C_{1-6} alkylcarbonyloxy group, a C_{1-6} alkylcarbonylamino group, a C_{1-6} alkylcarbonyl- C_{1-6} alkylamino group, a C_{1-6} alkyloxy group, a C_{1-6} alkyloxycarbonyl group, a C_{1-6} alkyloxycarbonylamino group, a C_{1-6} alkyloxycarbonyl- C_{1-6} alkylamino group, a C_{1-6} alkylamino group, a di- C_{1-6} alkylamino group, a sulfamoyl group, a C_{1-6} alkylsulfamoyl group, a di- C_{1-6} alkylsulfamoyl group, a sulfamoylamino group, a C_{1-6} alkylsulfamoylamino group, a di- C_{1-6} alkylsulfamoylamino group, a C_{1-6} alkylsulfamoyl- C_{1-6} alkylamino group, a di- C_{1-6} alkylsulfamoyl- C_{1-6} alkylamino group, a sulfamoyloxy group, a C_{1-6} alkylsulfamoyloxy group, a di- C_{1-6} alkylsulfamoyloxy group, a carbamoyl group, a C_{1-6} alkylcarbamoyl group, a di- C_{1-6} alkylcarbamoyl group, a carbamoylamino group, a C_{1-6} alkylcarbamoylamino group, a di- C_{1-6} alkylcarbamoylamino group, a C_{1-6} alkylcarbamoyl- C_{1-6} alkylamino group, a di- C_{1-6} alkylcarbamoyl- C_{1-6} alkylamino group, a carbamoyloxy group, a C_{1-6} alkylcarbamoyloxy group, a di- C_{1-6} alkylcarbamoyloxy group, a C_{1-6} alkylsulfonyl group, a C_{1-6} alkylsulfonylamino group, and a C_{1-6} alkylsulfonyloxy group; or a pharmaceutically acceptable salt thereof.

30. (New) The compound of Claim 29 wherein A^4 is $-N-$, A^1 is $-C(R_5)-$, A^2 is $-C(R_5)-$ and A^3 is $-C(R_5)-$.

31. (New) The compound of Claim 29 wherein A⁵ is -C(R₆)-, A⁶ is -C(R₆)-, A⁷ is -C(R₆)- and A⁸ is -C(R₆)-.
32. (New) The compound of Claim 29 wherein A⁷ is -N-, A⁵ is -C(R₆)-, A⁶ is -C(R₆)-, and A⁸ is -C(R₆)-.
33. (New) The compound of Claim 29 wherein R₆ is selected from a hydrogen atom, a fluorine atom, a chlorine atom, a methyl group, an ethyl group, an isopropyl group, a trifluoromethyl group, a methylcarbonyl group, a methoxymethyl group, a formyl group and a cyano group.
34. (New) The compound of Claim 29 wherein R₁ and R₁' are selected from a hydrogen atom, a hydroxyl group, a methyl group, a methoxy group, a methylsulfonylamino group and a methylcarbonylamino group.
35. (New) The compound of Claim 29 wherein R₁ and R₁' together form an oxo group or an ethylene-ketal group.
36. (New) The compound of Claim 29 wherein R₂ and R₂' are both hydrogen atoms.
37. (New) The compound of Claim 29 wherein R₂ and R₂' together form -CH₂CH₂-.
38. (New) The compound of Claim 29 wherein R₃ and R₃' are selected from a hydrogen atom, a hydroxyl group, a fluorine atom, a methoxy group, a methyl group, a hydroxymethyl group, a fluoromethyl group, a methanesulfonylaminomethyl group, a methanesulfonylmethylaminomethyl group, a methoxycarbonylaminomethyl group and a dimethylsulfamoylaminomethyl group.
39. (New) The compound of Claim 29 wherein R₄ is selected from a hydrogen atom, a fluorine atom, a chlorine atom, a methyl group, an ethyl group, a cyano group, a formyl group and a trifluoromethyl group.
40. (New) The compound of Claim 29 wherein R₄ and R₇ together form -CH₂-O-, -CH(CH₃)-O-, -C(CH₃)₂-O- or -N(CH₃)-CH₂-.
41. (New) The compound of Claim 29 wherein Z is -C(R₇)-, and R₇ is selected from a hydrogen atom, a fluorine atom and a methyl group.
42. (New) The compound of Claim 29 wherein X is -CH₂-, -O- or -N(CH₃)-.

43. (New) The compound of Claim 29 wherein n is 0.

44. (New) The compound of Claim 29 wherein n is 1 and Y is -CH₂-.

45. (New) A compound which is selected from the group consisting of:

(7R,9S)-7-(spiro[8-aza-bicyclo[3.2.1]octa-3,1'(3'H)-isobenzofuran]-8-ylmethyl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-9-ol;

(6R,8S)-6-(spiro[isobenzofuran-1-(3H),4'-piperidin]-1'-ylmethyl)-5,6,7,8-tetrahydroquinolin-8-ol;

(7R,9S)-7-[(3R*,4R*)-3-hydroxy-4-o-tolyl-piperidin-1-ylmethyl]-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-9-ol;

(7R,9S)-7-[(3R*,4R*)-(4-fluoro-o-tolyl)-3-hydroxypiperidin-1-ylmethyl]-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-9-ol;

(7R,9S)-7-(6'-aza-5'-fluoro-spiro[8-aza-bicyclo[3.2.1]-octa-3,1'(3'H)-isobenzofuran]-8-ylmethyl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-9-ol;

(6R,8S)-6-(3,3-dimethyl-spiro[isobenzofuran-1(3H),4'-piperidin-1'-ylmethyl]-5,6,7,8-tetrahydro-quinolin-8-ol;

(7R,9S)-7-(1-methylspiro-[2,3-dihydro-1H-indol-3,4'-piperidin]-1'-ylmethyl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-9-ol;

(6R,8S)-6-[4-(2-chlorophenyl)-4-fluoropiperidin-1-ylmethyl]-5,6,7,8-tetrahydroquinolin-8-ol;

(7R,9S)-7-[(3R*,4R*)-4-(2-chlorophenyl)-3-hydroxypiperidin-1-ylmethyl]-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-9-ol;

(7R,9S)-7-[(3R,4R)-4-(2-chloro-4-fluorophenyl)-3-hydroxypiperidin-1-ylmethyl]-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-9-ol;

(6R,8S)-6-[(3R,4R)-4-(2-chloro-4-fluorophenyl)-3-hydroxypiperidin-1-ylmethyl]-5,6,7,8-tetrahydroquinolin-8-ol;

(7R,9S)-7-[(3R*,4S*)-3-hydroxymethyl-4-phenyl-piperidin-1-ylmethyl]-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-9-ol;

(7R,9S)-7-[(3R*,4S*)-3-methyl-4-phenylpiperidin-1-ylmethyl]-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-9-ol;

N-{(7R,9S)-7-[(3R,4R)-4-(2-chloro-4-fluorophenyl)-3-hydroxypiperidin-1-ylmethyl]-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-9-yl}methanesulfonamide;

(6R,8S)-6-[(5'-fluoro-3',3'-dimethyl-3'H-6'-azaspiro[8-azabicyclo[3.2.1]octane-3,1'-isobenzofuran]-8-yl)methyl]-5,6,7,8-tetrahydroquinolin-8-ol; and

(6R,8S)-6-[(1S*,2R*,3R*)-3-(2-chloro-4-fluorophenyl)-2-hydroxy-8-azabicyclo[3.2.1]octan-8-ylmethyl]-5,6,7,8-tetrahydroquinolin-8-ol;
or a pharmaceutically acceptable salt thereof.

46. (New) A compound which is selected from the group consisting of:

(7R,9S)-7-[(3R*,4R*)-3-hydroxy-4-o-tolyl-piperidin-1-ylmethyl]-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-9-ol;

(7R,9S)-7-[(3R*,4R*)-(4-fluoro-o-tolyl)-3-hydroxypiperidin-1-ylmethyl]-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-9-ol;

(7R,9S)-7-(6'-aza-5'-fluoro-spiro[8-aza-bicyclo[3.2.1]-octa-3,1'(3'H)-isobenzofuran]-8-ylmethyl)-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-9-ol;

7R,9S)-7-[(3R*,4R*)-4-(2-chlorophenyl)-3-hydroxypiperidin-1-ylmethyl]-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-9-ol;

6R,8S)-6-[(3R,4R)-4-(2-chloro-4-fluorophenyl)-3-hydroxypiperidin-1-ylmethyl]-5,6,7,8-tetrahydroquinolin-8-ol;

N-[(7R,9S)-7-[(3R,4R)-4-(2-chloro-4-fluorophenyl)-3-hydroxypiperidin-1-ylmethyl]-6,7,8,9-tetrahydro-5H-cyclohepta[b]pyridin-9-yl]methanesulfonamide;

(6R,8S)-6-[(5'-fluoro-3',3'-dimethyl-3'H-6'-azaspiro[8-azabicyclo[3.2.1]octane-3,1'-isobenzofuran]-8-yl)methyl]-5,6,7,8-tetrahydroquinolin-8-ol;

(6R,8S)-6-[(1S*,2R*,3R*)-3-(2-chloro-4-fluorophenyl)-2-hydroxy-8-azabicyclo[3.2.1]octan-8-ylmethyl]-5,6,7,8-tetrahydroquinolin-8-ol;
or a pharmaceutically acceptable salt thereof.

47. (New) A pharmaceutical composition which comprises an inert carrier and a compound of Claim 20, or a pharmaceutically acceptable salt thereof.

48. (New) A method for treating a disease or disorder selected from the group consisting of: pain; tolerance to a narcotic analgesic; dependence on or addiction to a narcotic analgesic; obesity; impaired cognition; dementia or amnesia; cerebrovascular disease; Alzheimer's disease; attention deficit hyperactivity disorder; learning disability; schizophrenia; neurodegenerative diseases; Parkinsonism; chorea; depression; affective disorder; diabetes insipidus; polyuria; and hypotension, in a mammalian patient in need thereof which comprises administering to the patient a therapeutically effective amount of the compound of Claim 20, or a pharmaceutically acceptable salt thereof.